EDITORIAL

Severe Acute Respiratory Syndrome Coronavirus 2 Nosode: A Potential Alternative Vaccine Platform

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Abstract

Besides conventional vaccinations, viable alternatives are needed to elicit an immune response against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). We propose and highlight the value of a homeopathic approach known as the "nosode" for the prevention of coronavirus disease-2019 (COVID-19). Nosode is an extract prepared from disease-affected tissues which is subsequently processed and administered as an antidote for the same medical condition. This concept might be a crucial therapeutic approach for viral infections since infected tissues contain a wide range of important viral antigens that could induce a functional host response via immunological sensitization. Thereby, nosode preparation produced from SARS-CoV-2-affected tissues may provide protection against COVID-19. "SARS-CoV-2 nosode" warrants more scientific investigation as a viable alternative vaccination platform.

Keywords: COVID-19, Nosode, SARS-CoV-2, Variolation.

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As of March 13, 2022, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus has infected around 455 million and claimed around 6 million lives worldwide.[1] Although several pharmacological agents claimed benefit against coronavirus disease-2019 (COVID-19), the "vaccination" remains the best option in preventing COVID-19 and its completion. Considering the preventive measure, some countries have achieved faster vaccination rates, whereas other countries suffered due to their higher population, inadequate vaccine supply, and lack of awareness. As timely vaccine production becomes challenging, feasible alternatives are always recommended for any pandemic situation including SARS-CoV-2. In this context, it is appropriate to discuss about "nosode" an alternative homeopathy treatment approach. Nosode is fundamentally known as an extract prepared from biological samples (infected or diseased tissues, or pathogens), diluted, and given to prevent or treat the certain medical condition.[2,3] Nosode is applicable in the management of infectious diseases, as the biological extract contains critical antigens that stimulate host response through immune sensitization. In the past, highly diluted leptospirosis was administered on a large scale for epidemic control.[4] Interestingly, experimental mice with nosode pretreatment showed significant response to infection against pathogens like *Plasmodium berghei* and *Trypanosoma cruzi*.[5,6]

Considering the evidence mentioned above, it is worth speculating similar concept of optimal exposure to SARS-CoV-2 may protect against COVID-19. Few successful studies were lined up to support the rationale in proposing SARS-CoV-2 nosode. Interestingly, the practice of face masking results in the "variolation" phenomenon and serves protective role beyond the conventional expectation of reduced transmission of the SARS-CoV-2.[7] As a result of such infection control barriers, there is minimal SARS-CoV-2 exposure, which reduces disease severity with more asymptomatic cases found in several settings. For instance, more asymptomatic cases (81%) were found on the Argentinian cruise that followed universal masking measures than the Diamond Princess cruise that did not follow these measures and reported a relatively lower number of asymptomatic cases (17.9%).[7,8] Similarly, in other settings such as seafood processing plant and a chicken plant with the regular mark usage, the rate of asymptomatic infections remained as high as 95%.[8] Likewise, viral inoculation experiments in Syrian hamsters indicate that lower degree of exposure to SARS-CoV-2 reduces disease severity.[9]

The development of the Variola vaccine and the eventual eradication of smallpox is an age-old but brilliant example of variolation.[10] Although such a phenomenon can be potentially explored in the context of viral infections, it is not practiced due to the risk involved with iatrogenic inoculation.[11] Despite implementation of stringent infection control measures, like social distancing, mask use, and hand sanitization, there is continuous environmental exposure to the inactivated viruses or virus-related disintegration products (like the spike protein) which may confer some degree of passive immunity against COVID-19.[12] However, viruses cannot be tinkered for the purpose of controlled exposure. It is vital to deploy a potential alternative strategy like "SARS-CoV-2 nosode" that could enormously benefit.

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The COVID-19-affected (i.e., SARS-CoV-2 infected) tissues like the lungs which show a higher viral distribution [as a result of angiotensin-converting enzyme 2 (ACE-2) expression] remain as the major hot spots of the ACE-2 binding SARS-CoV-2 virus;[13,14] such tissues could be reliably used for nosode preparation. On the contrary, blood samples of SAR-CoV-2-positive donors are also compatible for nosode preparation. Once the tissues are collected, they need to be carefully processed and prepared into a therapeutic "nosode." In ideal conditions, the inactivated virions and viral proteins within the nosode could generate a relevant immune response in the healthy individual, which could confer COVID-19 protection (passive immunity). In this manner, the deceased patient's tissue can also be the alternate source for the preparation of SAR-CoV-2 nosode. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) nosode is conceptually comparable to plasma therapy, where the donor's antibodies eventually protect the recipient. Unlike convalescent plasma that contains a range of antibodies, nosode on the other hand contains the whole spectrum of inactivated virus and virus-associated antigens (including and not limited to the spike proteins), capable of developing a relevant response against SARS-CoV-2 infection. However, efforts are needed to determine the optimal potency capable of triggering a healthy immune (humoral or cell-mediated) response.[15]

Additionally, it would also be useful to design a universal nosode protocol (applicable for different tissues). Because the virus's structural integrity and infective capabilities are destroyed during the nosode preparation (achieved through the use of chemical agents such as alcohol), the viral mixture inside the final preparation should ideally just be a potential vaccine capable of eliciting an immune response. Also, the administration routes of final preparation could be open wounds or mucosa or simply breathing it via aerosolized preparations (mimicking an infection) to acquire significant immunological response. Although there are advantages of SAR-CoV-2 nosode, inability to scale up is a limitation because nosode approach relies on the availability of natural samples containing virus or virus particles after tissue clearance by host mechanisms. Few initiatives have been documented in preparation of nosode sourced from an oropharyngeal swab of a SARS-CoV-2-positive patient.[16,17] It is worth noting that the SARS-CoV-2 nosode is still in the conceptual stage, and further preparations, *in vitro* research, animal tests, and clinical trials are required. This strategy can be postulated as a preventative measure, as the level of protection may not be equal to a traditional vaccine. Overall, the alternative vaccine approach provided here has not been dealt with in the mainstream SARS-CoV-2 vaccinology, yet it is well within its scope. This technique combines the pioneering achievements of Sir Edward Jenner (the inventor of the first vaccine) and the homeopathic idea of "nosode." The SARS-CoV-2 nosode is an option worthy of further scientific investigation.

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